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OCCUPATIONAL RISKS OF BLADDER CANCER AMONG WHITE WOMEN IN THE UNITED STATES

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The relation between occupation and bladder cancer in women was examined based on data collected during the National Bladder Cancer Study, a population-based, case-control study conducted in 10 areas of the United States. Occupational hazards among women have received little attention in previous bladder cancer studies, in part because most studies have included too few females to accurately estimate risks. In this large case-control study, 652 white female bladder cancer patients and 1,266 white female controls were interviewed to obtain lifetime occupational histories. Patterns of bladder cancer risk by occupation in women tended to be similar to those previously observed among men. Increased risk was apparent for women ever employed in metal working and fabrication occupations (relative risk (RR) = 1.5; 95% confidence interval (CI) 0.9–2.6). Within this summary occupation category, punch and stamping press operatives had a significant trend in risk with increasing duration of employment ($p = 0.012$); the RR for women employed 5 years or more was 5.6 (95% CI 1.4–26.4). The authors also observed an increased risk for women employed as chemical processing workers (RR = 2.1; 95% CI 0.9–5.1 = with a significant, positive trend in risk with increasing duration of employment ($p = 0.042$). In contrast, a decreased risk was apparent for female textile workers (RR = 0.6; 95% CI 0.3–1.1) with a significant, negative trend in risk with increasing duration of employment ($p = 0.031$); the relative risk for textile workers employed 10 years or more was 0.4. The authors estimate that 11% of bladder cancer diagnosed among white women in the United States is attributable to occupational exposures; this percentage is considerably lower than the 21–25% previously reported for white men in this study.

bladder neoplasms; occupations; women

Occupational cancer hazards among women have received little attention, even in studies of bladder cancer, a site with one of the most well-established occupational

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Abbreviations: CI, confidence interval; RR, relative risk.

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etiologies (1). This study investigates the relation between occupation and bladder cancer in women based on data collected as part of the National Bladder Cancer Study, a population-based, case-control study conducted in 10 areas of the United States.

Previous studies have typically lacked adequate numbers of women to accurately estimate occupational risks. Our data derive from interviews with 652 white female cases and 1,266 white female controls, the largest study of occupation and bladder cancer among women conducted to date. This large size provided the opportunity to estimate occupational risks with more precision than in previous studies, as well as to compare these risks with those previously reported for men in our study (1, 2).

Materials and methods

The case series consisted of all incident cases of carcinoma of the urinary bladder that were histologically confirmed during a 1-year period that began in late 1977 among 21- to 84-year-old residents of the states of New Jersey, Connecticut, Iowa, New Mexico, and Utah and the cities of Atlanta, Georgia; Detroit, Michigan; New Orleans, Louisiana; San Francisco, California; and Seattle, Washington.

Of the 1,070 female cases identified for study, interviews were obtained for 733 cases (69 percent). Sixty patients had physicians who refused permission for interview, 22 could not be located, 75 refused to cooperate, 104 were too ill to be interviewed, 75 had died, and one could not speak English.

The control series was selected from the general population of the study areas and frequency matched to cases on age (within 5 years) and geographic area. For each case, approximately two controls were chosen. Controls aged 21–64 years were selected using a method of random digit dialing (3). Those aged 65–84 years were selected by random sampling from the Health Care Financing Administration's lists of residents aged 65 years or older in each study area.

Of the 1,852 female controls identified for study, interviews were obtained for 1,500 subjects (81 percent). Forty-four controls could not be located, 223 refused to participate, 63 were too ill to be interviewed, 17 had died, two could not speak English, and three could not be interviewed for other reasons. For additional information on response rates, see Hartge et al. (4).

The study group was further limited to white women because there were too few nonwhite women (40 cases and 122 controls) for satisfactory analysis. In addition, 35 cases and 104 controls were excluded because they never held a job for at least 6 months, and six cases and eight controls were excluded because their interviews were judged to be unreliable. In total, there were 652 white female cases and 1,266 white female controls included in this analysis.

In-person interviews were conducted by a trained interviewer with a standardized questionnaire. The questionnaire was structured to elicit detailed information on every job a subject had held for at least 6 months since the age of 12 years. To code data on industry and job title, we used the alphabetic index of industry and occupations of the US Bureau of the Census (5). To make our analysis more exposure oriented, we recoded the data according to a two-step process: 1) Workers within each industry were grouped by occupational code, and 2) occupational codes were grouped by potential for similar exposure. For example, we grouped checkers, examiners, inspectors, and graders within the rubber products manufacturing industry because they probably have similar exposures but very different census codes, reflecting their varying levels of skill. Based on this approach, a total of 417 census codes were transformed into 163 occupational categories that were meaningful for analysis. Data by original census code are available on request. In addition, we also grouped workers involved in processing jobs within a specific industry into a single category. This technique was especially

useful for several occupations, such as rubber processing worker and chemical processing worker. The questionnaire also included items on smoking history, coffee consumption, artificial sweetener use, residential history, source of water, fluid intake, hair dye use, and medical history.

The association between occupation and the incidence rate of bladder cancer was quantified by the "relative risk" (RR) as estimated by the odds ratio. The risk for women employed in each occupation was estimated relative to the risk for women "never employed" in that occupation. Relative risks were adjusted by the method of maximum likelihood (6). Initially, we stratified the data by age, smoking, employment in other high-risk occupations, geographic area, education, source of drinking water, and birthplace. There was, however, little confounding in these data. The only factor for which adjustment had a consistent effect on the relative risk estimates was smoking (in five categories); thus, all relative risks are adjusted for smoking. In addition, relative risks are also adjusted for any other factor that had a confounding effect on the point estimate for a specific occupation (see table 2). Two-sided 95 percent confidence intervals (CIs) for the adjusted estimates of relative risk were calculated by the interval estimation procedure of Gart (6). An increased or decreased risk was considered statistically significant when the 95 percent CI did not include the null value. Two-tailed significance tests for trend were calculated by the Mantel extension of the Mantel-Haenszel procedure (7). Population attributable risks were estimated by the method of Whittemore (8) and were adjusted for age, geographic area, and smoking. Two-sided 95 percent CIs for the adjusted population attributable risk were also computed according to the method of Whittemore (8).

Because a large number of occupations have been included in this analysis, it is not possible to present all the results from this study. Thus, results are presented if they are based on at least 15 exposed women and satisfy at least one of the following criteria: 1) workers in the occupation experienced a statistically significant, increased or decreased risk; 2) any occupation category suspected a priori with a relative risk of at least 1.3, regardless of statistical significance (an occupation was considered to be "a priori suspect" if workers in that occupation have experienced increased risk in at least one previous study); 3) any occupation category with a relative risk of at least 1.5, or less than or equal to 0.6, regardless of statistical significance; or 4) the occupation was a summary category. In a few instances, results are also presented for an occupation in which less then 15 women had worked if the occupation was suspected a priori. Thirty-one of 144 occupation categories met at least one of these criteria.

RESULTS

White female cases and controls were comparable with regard to several descriptive factors pertaining to occupation, including total number of years employed, age started working, number of industries and occupations ever employed in, and number of jobs ever held (table 1). Cases and controls were also comparable with regard to several other factors, including education (mean years, 11.1 and 11.0 for cases and controls, respectively) and urbanicity (84 percent of cases and 81 percent of controls had an urban area as their usual lifetime residence).

In contrast, cases and controls were dif-

TABLE 1

Comparison of cases and controls by employment patterns, white females: National Bladder Cancer Study

Occupational factor	Mean	
	Cases	Controls
No. of years employed	24.2	24.3
Age started working	20.9	21.1
No. of industries	3.0	3.0
No. of occupations	3.0	3.0
No. of jobs	4.3	4.3
No. of subjects	652	1,266

ferent with regard to their smoking habits; smoking was clearly related to risk in white women. The age-adjusted relative risks by amount smoked were 1.0 for nonsmokers, 2.2 for women who smoked less than one pack/day, 2.4 for women who smoked one to less than two packs/day, and 3.1 for women who smoked two or more packs/day.

Occupations suspected a priori

Table 2 shows relative risks for all a priori suspect occupations. Occupations with summary categories are presented first along with subcategories for which workers had a relative risk of at least 1.3, or less than or equal to 0.6. These are followed by some miscellaneous, specific occupations that did not fit easily into a summary category.

Of the occupations suspected a priori, rubber processing worker was the only occupation in which women had a statistically significant increased risk (RR = 4.5; 95 percent CI 1.1–21.9), although this estimate was based on small numbers. Nonsignificant increased risks (i.e., RR ≥ 1.3) were apparent for the following 11 previously suspected occupations: painter; machine operative, not elsewhere classified; welder

TABLE 2

Numbers of cases and controls ever employed in each a priori suspect occupation category and relative risks, white females: National Bladder Cancer Study*

Occupation title	Cases†	Controls†	Relative risk‡	95% confidence interval
Summary printer	1	10	0.2	<0.1–1.4
Summary painter	9	12	1.5	0.6–4.0
Summary driver of motor vehicles	9	12	1.1	0.4–3.0
Summary metal machinery worker	87	122	1.4	1.0–1.9
Machine operative, NEC§	75	107	1.3	1.0–1.9
Summary welder, flame-cutter, solderer	10	19	0.7‖	0.3–1.7
Welder and flame-cutter	6	6	1.7	0.5–6.0
Summary metal working and fabrication	31	35	1.5	0.9–2.6
Punch and stamping press operative	12	13	1.7	0.7–4.0
Metal fabrication, assembly, repair worker	11	7	2.5	0.9–7.4
Summary saleswoman and sales manager	164	296	1.1	0.9–1.4
Auctioneer, peddler	9	26	0.6	0.2–1.3
Saleswoman and salesclerk, NEC	14	11	2.5	1.0–6.0
Summary paper processing worker	8	10	1.6	0.6–4.6
Paperboard container and box worker	7	8	1.9	0.6–6.0
Summary cook, baker, food counter worker	56	112	1.0	0.7–1.4
Summary food service worker	92	155	1.0	0.8–1.4
Summary actor, artist, musician, writer	9	21	0.9	0.4–2.2
Miscellaneous occupations suspected a priori				
Textile worker	14	50	0.6	0.3–1.1
Rubber processing worker	8	3	4.5	1.1–21.9
Chemical processing worker	13	12	2.1	0.9–5.1
Auto worker	7	6	2.1	0.6–7.5
Hairdresser	17	20	1.4	0.7–2.9
Dry cleaner, ironer, presser	23	32	1.4	0.8–2.5
Medical technician	6	18	0.5	0.2–1.4

* An a priori suspect occupation was defined to be any occupation in which workers have been reported to have increased risk in at least one previous study.

† Ever employed in each occupation.

‡ For each occupation, relative to a risk of 1.0 for females never employed in that occupation. Smoking-adjusted relative risks are given in every instance, unless otherwise specified.

§ NEC, not elsewhere classified.

‖ Adjusted for smoking and employment in other high-risk occupations.

and flame-cutter; punch and stamping press operative; metal fabrication, assembly, and repair worker; saleswoman and salesclerk, not elsewhere classified; paperboard container and box worker; chemical processing worker; auto worker; hairdresser; and dry cleaner, ironer, and presser. Nonsignificant, decreased risks (i.e., RR $\leq$ 0.6) were seen for the following previously suspected occupations: printer, auctioneer and peddler, textile worker, and medical technician.

Newly identified high- and low-risk occupations

Occupations not previously suggested as high risk in which women experienced elevated risk (i.e., RR $\geq$ 1.5) are presented in table 3. Of the newly identified high-risk occupations, no statistically significant elevated risks were apparent. Nonsignificant excesses were observed for three occupations: checker, examiner, and inspector in manufacturing, not elsewhere classified; cutting operative; and dishwasher.

Women in five occupational groups had decreased relative risks (i.e., RR $\leq$ 0.6) (table 3): manufacturing foremen, not elsewhere classified; restaurant and bar managers; recreation workers; bill collectors and insurance adjusters; and editors, reporters, and proofreaders. No statistically significant, decreased risks were observed, however.

Temporal factors

We examined the relation between bladder cancer risk and duration of employment for each occupational category with an overall relative risk of at least 1.0, as well as for those that were a priori suspect. There were six occupations where a significant, positive trend in risk with increasing duration was apparent (table 4). Of these, the trend was consistent, as well as significant, for only three occupations—punch and stamping press operative, chemical processing worker, and saleswoman and salesclerk, not elsewhere classified. In contrast, we observed a consistent and significant, negative trend in risk with increasing duration of employment as a textile worker (table 4).

Population attributable risks

A basic problem in estimating the population attributable risk for occupation is defining "occupational risk." We estimated

TABLE 3

Numbers of cases and controls employed in each newly identified high- and low-risk occupation category and relative risks, white females: National Bladder Cancer Study*

Occupation title	Cases†	Controls†	Relative risk‡	95% confidence interval
Newly identified high-risk occupations				
Checker, examiner, inspector, manufacturing, NEC§	50	64	1.5	1.0–2.3
Cutting operative	11	13	1.6	0.7–4.0
Dishwasher	9	10	1.8	0.7–4.9
Newly identified low-risk occupations				
Manufacturing foreman, NEC	9	25	0.6	0.3–1.5
Restaurant and bar manager	7	23	0.5	0.2–1.2
Recreation worker	4	14	0.6	0.2–1.8
Bill collector, insurance adjuster	8	24	0.6	0.2–1.4
Editor and reporter, proofreader	3	14	0.4	0.1–1.4

* See Materials and Methods for definition.

† Ever employed in each occupation.

‡ For each occupation, relative to a risk of 1.0 for females never employed in that occupation. Smoking-adjusted relative risks are given in every instance.

§ NEC, not elsewhere classified.

TABLE 4

Numbers of cases and controls and relative risks according to duration of employment in specified occupations, white females: National Bladder Cancer Study*

Occupation title	Duration (years)	Cases	Controls	Relative risk†	Trend test (p value)
Machine operative, NEC‡	<5	40	63	1.2	0.048
	5–14	25	27	1.7	
	≥15	8	14	1.0	
Punch and stamping press operative	<5	3	8	0.6	0.012
	≥5	9	3	5.6	
Metal fabrication, assembly, repair worker	<5	9	4	3.5	0.021
	≥5	2	2	2.1	
Chemical processing worker	<5	7	7	1.9	0.042
	≥5	6	5	2.2	
Checker, examiner, inspector, manufacturing, NEC	<5	28	34	1.5	0.029
	≥5	22	28	1.5	
Saleswoman and salesclerk, NEC	<10	8	8	2.0	0.018
	≥10	5	3	3.0	
Textile worker	<5	6	19	0.6	0.031
	5–9	5	15	0.7	
	≥10	3	14	0.4	

* Females with unknown duration of employment were excluded.

† For each level of duration of employment in the specified occupation, relative to a risk of 1.0 for females never employed in that occupation, adjusted for smoking and age.

‡ NEC, not elsewhere classified.

the population attributable risks for occupation using several definitions and selected one set of estimates for presentation. These estimates were based on defining occupational risk as employment in any previously suspected occupation with a relative risk of at least 1.1 or in any occupation with a relative risk of at least 1.5 or with a significant duration effect. Previously suspected occupations with a relative risk of less than 1.1 did not explain any excess risk in our data and, thus, were excluded. These population attributable risk estimates were virtually identical to those based on defining occupational risk as simply employment in a previously suspected occupation with a relative risk of at least 1.1.

The population attributable risk for occupation in white women was 11 percent (95 percent CI 3–19 percent). This estimate was substantially higher for women aged less than 65 years (population attributable risk = 19 percent; 95 percent CI 7–31 percent) than for those aged 65-84 years (population attributable risk = 5 percent; 95 percent CI −5 to 16 percent).

DISCUSSION

Our findings indicate that patterns of bladder cancer risk by occupation among women are generally similar to those previously observed among men in this study (1, 2) and in other studies.

Increased risk was apparent for women ever employed in metal working and fabrication occupations (RR = 1.5; 95 percent CI 0.9–2.6). Within this summary occupation category, punch and stamping press operatives had a significant trend in risk with increasing duration of employment (p = 0.012); the RR for women employed 5 years or more was 5.6 (95 percent CI 1.4–26.4). Metal fabrication, assembly, and re-

pair workers also experienced an elevated risk (RR = 2.5; 95 percent CI 0.9–7.4) and a significant trend in risk with increasing duration of employment ($p = 0.021$), although this trend was not consistent. Male metal workers have experienced increased bladder cancer risk in 11 previous studies (9–19) and in our study (1). This is the first report of an excess risk among female metal workers.

We also observed an elevated risk for women employed as chemical processing workers (RR = 2.1; 95 percent CI 0.9–5.1) with a significant, positive trend in risk with increasing duration of employment ($p = 0.042$). A small increased risk was also seen for white male chemical processing workers in our study (RR = 1.2; 95 percent CI 0.8–1.7) (1) as well as in several other studies (20). It is unclear whether the higher risk seen for women compared with men chemical processing workers is due to chance or whether it reflects differences in exposure between men and women chemical processing workers.

Increased risks previously observed for men in our study (1, 2) and in other studies were also observed for women employed in several other occupations, i.e., painter (21, 22); machine operative (18, 23); welder and flame-cutter (16); paperboard container and box worker (24); rubber processing worker (25, 26); hairdresser (27); and dry cleaner, ironer, and presser (28, 29). The increased risk observed for rubber processing workers, however, was the only statistically significant increase.

Conflicting results for women and men were apparent for salespersons and salesclerks. Saleswomen and female salesclerks had an increased risk (RR = 2.5; 95 percent CI 1.0–6.0) and a significant, positive trend with increasing duration of employment ($p = 0.018$), whereas salesmen and male salesclerks did not experience increased risk (1, 2). There have been only two previous reports of an elevated risk for salesmen (23, 30), and no plausible biologic explanation for this elevation is apparent. Thus, it appears that the observed increased risk in saleswomen and female salesclerks may have been due to chance.

In contrast, a decreased bladder cancer risk was apparent for female textile workers (RR = 0.6; 95 percent CI 0.3–1.1). A significant, negative trend in risk with increasing duration of employment was observed ($p = 0.031$); the relative risk for textile workers employed 10 or more years was 0.4. We previously observed a significant, decreased risk for white male textile workers in our study (RR = 0.6; 95 percent CI 0.4–0.9) (1), with a significant, negative trend in risk with increasing duration of employment ($p = 0.006$) (Silverman, National Cancer Institute, unpublished data, 1989). Decreased risks were apparent among both women and men textile workers who were nonsmokers (RR = 0.6 and 0.6, respectively) and, thus, were probably not due to negative confounding by smoking.

Within the textile worker category, deficits in risk were apparent in every subgroup of textile worker. For women textile workers, relative risks were 0.5 (95 percent CI 0.2–1.3) for spinners, twisters, and winders; 0.5 (95 percent CI 0.1–2.5) for weavers; 0.7 (95 percent CI 0.1–4.4) for knitters, loopers, and toppers; and 0.3 (95 percent CI 0.1–1.6) for textile operatives, not elsewhere classified. Similar decreased risks were observed for men by type of textile work.

Results of some previous studies of bladder cancer have suggested that textile workers may have an increased risk for both women (10, 12, 13, 31, 32) and men (10, 14, 23, 33), whereas textile workers in other studies experienced no excess risk (22, 34). It is noteworthy that, in studies of lung cancer, cotton textile workers appear to have a decreased risk (35). Unfortunately, we were unable to determine whether our textile workers were primarily exposed to cotton.

It is unclear whether the observed reduced risk for textile workers was due to chance or reflects a real protective effect. Because this is the first report of a reduced bladder cancer risk among textile workers, it will require substantial confirmation be-

fore any interpretation of a protective effect can be made.

This study has a number of limitations. 1) Differential response rates between cases and controls may have resulted in nonresponse bias. It is unlikely that nonresponse bias had a significant impact on our results because all point estimates were evaluated for confounding due to socioeconomic status as measured by education and were adjusted for socioeconomic status when necessary. It was not possible, however, to determine if there were other occupationally related reasons for nonresponse. 2) Because of the large number of comparisons made in this analysis, some findings were probably due to chance. For this reason, we considered the following four factors to distinguish true high-risk occupations from chance effects: magnitude of risk, statistical significance, duration-response relation, and consistency with results from previous epidemiologic studies. 3) It was not possible to identify the specific exposures responsible for observed increased risks. This will require in-depth industrial hygiene studies, which were beyond the scope of this case-control study.

Our estimate of the population attributable risk for occupation among white women in the United States was 11 percent. This estimate is considerably lower than the 21–25 percent previously reported for white men (1). This difference was due to the lower proportion of women compared with men ever employed in "high-risk" occupations (40 and 80 percent, respectively). The length of a woman's working life in our study was, on average, 20 years shorter than that of a man's, providing women less opportunity to work in a high-risk occupation. By contrast, women and men experienced similar magnitudes of risk associated with employment in high-risk occupations (RR = 1.4 and 1.5, respectively). Thus, occupational risk of bladder cancer appears to be similar for women and men, although the rate of exposure to occupational carcinogens is lower in women.

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